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ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005

EXAMINER	
YANG, NELSON C	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/901,121	CHU, WEI-SING	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-58,61,64-66,68 and 69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-58,61,64-66,68 and 69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's amendments of claims 38, 39, 42, 43, 44, 47, 48, 53-57, 64, 66, and 68 are acknowledged and have been entered.

2. Applicant's cancellation of claims 59, 60, 62, 63, and 67 is acknowledged and has been entered.

3. Claims 48-58, 61, 64-66, 68 and 69 are pending.

Rejections Withdrawn

4. Applicant's arguments, see page 7, filed March 25, 2004, with respect to the objections of claims have been fully considered and are persuasive. The objection of claims 41 and 66 has been withdrawn.

5. Applicant's arguments, see page 7, filed March 25, 2004, with respect to the rejection of claims 38-69 under 35 U.S.C. 112, second paragraph have been fully considered and are persuasive. The rejection of claims 38-69 under 35 U.S.C. 112, second paragraph has been withdrawn.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 50, 52, 64 and 65 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. It is unclear how multiple head or multiple intensities would be used in order to perform immunohistochemistry, in situ hybridization, fluorescent in situ hybridization, a Southern hybridization, a Northern hybridization or an ELISA. While applicant teach the use of multiple heads and intensities in ultrasound fixation or processing methods (p. 13-14), it is unclear how these would apply to methods of performing immunohistochemistry, in situ hybridization, fluorescent in situ hybridization, a Southern hybridization, a Northern hybridization or an ELISA.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 38-40, 43, 45-48, 56, 58-64 are rejected under 35 U.S.C. 102(b) as being anticipated by Lanza et al [US, 5,958,371].

Lanza et al teaches a method of performing hybridization on a solid phase using ultrasound with a frequency of at least 100 KHz. Specifically, Lanza teaches a method of performing hybridization on nitrocellulose membranes using ultrasound, with ultrasonic transducers suitable for biomedical and diagnostic applications within a frequency range of 5 to 50 MHz (column 7, lines 35-64).

10. With respect to claim 39, the solid phase is a tissue section. Specifically, the method is performed on a tissue surface (column 7, lines 35-40).

11. With respect to claim 40, the hybridization, annealing, or ELISA is performed on a membrane (column 7, lines 55-60).

12. With respect to claim 43, the frequency range used by Lanza et al is 5 to 50 MHz, which falls within the range of 100 KHz – 50Mhz (column 7, lines 35-64).

13. With respect to claim 45, the method is performed on a solid phase, where one or more ultrasound transducers are used to produce an ultrasound field (column 7, lines 35-64).

14. With respect to claim 46, Lanza et al teaches the use of a transducer that produces ultrasound (column 7, lines 35-64). Since the transducer head is simply the part of the transducer containing the transducer elements (see Kretz (US 4403509]), a person of ordinary skill in the art would clearly realize that the transducer Lanza et al teaches would be comprised of at least one head.

15. With respect to claim 47 and 48, Lanza et al teaches the use of a transducer that produces a broadband, or wideband, frequency (column 7, lines 55-64). Since the transducer head is simply the part of the transducer containing the transducer elements (see Kretz (US 4403509]), a person of ordinary skill in the art would clearly realize that the transducer Lanza teaches would inherently be comprised of at least one head.

16. With respect to claim 56, the method is performed on a solid phase that is rotated (column 10, example 4, column 17-18, example 10).

17. With respect to claim 58 and 60, the ultrasound is a continuous wideband frequency in the range of 0.1-50 MHz (column 7, lines 55-64).

18. With respect to claim 59, the ultrasound is a single frequency in the range of 0.1-50 MHz, specifically a 7.5 MHz focused transducer (column 9, example 3).

19. With respect to claim 61, the ultrasound is produced in pulses. Specifically, the ultrasound is operated in a pulse-echo mode (column 9-15, examples 4-7).

20. With respect to claim 62, Lanza et al teaches the use of a 7.5 MHz linear phased array transducer (columns 15-17, examples 8-9). Although Lanza et al doesn't specifically mention that the transducer produces pulses, a person of ordinary skill in the art would know that linear phased array transducers are composed of several hundred elements, with subgroups of adjacent elements producing pulses simultaneously.

21. With respect to claim 63, the ultrasound is produced as a wideband frequency in the range of 0.1-50 MHz. Specifically, the ultrasound is produced at 30-60 MHz (column 9-15, examples 4-7).

22. With respect to claim 64, the pulses vary in frequency in the range of 0.1-50 MHz (5-15 MHz) (column 14-15, example 7).

Claim Rejections - 35 USC § 103

23. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

24. Claims 41, 42, and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lanza et al [US 5,958,371] in view of Gravlee, Jr [US 3,961,097].

The method of Lanza et al as disclosed above fails to recite the specific feature of ultrasound receiving power in the range of 0.01-100 W/cm^2. However, Gravlee, Jr. teaches that

the intensity of ultrasound must be maintained at a level below the level at which damage to cells in the tissue occurs. It would have been obvious for a person of ordinary skill in the art to use an ultrasound receiving power within this particular range in order to avoid damaging the sample, because it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. At 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since applicant has not disclosed that the specific limitations recited in instant claims 41, 42, and 69 are for any particular purpose or solve any stated problem and the prior art teaches that improved noninvasive method for forming an acoustic contrast agent which can be targeted in vitro or in vivo and which when bound to a specific desired site alters the acoustic reflectivity of a tissue surface or support media in a manner detectable using ultrasonic transducers, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by Lanza et al by normal optimization procedures known in the art in order to avoid damaging the sample.

25. Claims 44, 51, 53-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lanza et al [US 5,958,371], in view of Blank [US 5,913,826] and Lang et al [US 5,941,825].

Lanza et al teaches a method involving the use of transducers to produce ultrasound (column 7, lines 35-64). Lanza et al does not specifically teach the use of two or more transducers to produce ultrasound.

26. Blank, however, teaches the use of a multiple transducer array in order to fit a three-dimensional contour (column 13, lines 19-29). Lang et al further teaches that the ultrasound system can contain three ultrasound sources transmitting at three different frequencies and separated by predetermined distances. Detection of returning signals can include sampling of all the returning frequencies at all detector sites, which effectively allows each ultrasound source to be coded and the returning signals can be identified with a particular ultrasound source. This permits greater refinement of reflective distances because the reflective distance from each ultrasound source is separately detected at each detector, which facilitates signal averaging and can optionally provide a basis of triangulation between different ultrasound sources and the reflective interfaces in order to verify reflective distances. This essentially permits detection from multiple reflective angles (column 24, lines 1-20). Therefore it would be obvious to use two or more transducers in the method disclosed by Lanza et al, in order to fit a three-dimensional contour or to permit detection from multiple reflective angles.

27. With respect to claim 51, although Lanza et al does not teach the step of having each transducer produce a different frequency, Lang et al teaches that ultrasound sources transmitting at different frequencies permits greater refinement of reflective distances because the reflective distance from each ultrasound source is separately detected at each detector, which facilitates signal averaging and can optionally provide a basis of triangulation between different ultrasound sources and the reflective interfaces in order to verify reflective distances (column 24, lines 1-

20). Therefore, it would be obvious to produce different ultrasound frequencies in the method of Lanza et al, in order to permit detection from multiple reflective angles.

28. With respect to claim 53, Lanza et al teaches the application of a range of frequencies to a sample (column 14-15, example 7).

29. With respect to claim 54, Lanza et al discloses a method where the transducers are arranged in a two-dimensional arrangement (columns 9-17, examples 4-9)

30. With respect to claim 55, although Lanza et al does not disclose a method where the transducers are arranged in a three-dimensional arrangement, Blank teaches it would be obvious to use multiple transducers in order to fit a three-dimensional contour. Therefore, it would be obvious to use multiple transducers arranged in a three-dimensional arrangement in the method disclosed by Lanza in order to fit a three-dimensional contour.

31. Claims 46-49, and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lanza et al [US 5,958,371], in view of Kretz [US 4,403,509].

While Lanza et al teaches the use of a transducer comprising of a head to produce ultrasound, he does not teach the use of a transducer with multiple heads (column 7, lines 35-64). Kretz, however, teaches that the use of multiple transducer heads will allow the entire image to have a higher resolution. (column 3, lines 7-30). Therefore it would be obvious to use a transducer with multiple heads in the method disclosed by Lanza et al, in order to achieve an image with higher resolution.

32. With respect to claims 47 and 48, Lanza et al teaches the use of transducers capable of emitting wideband frequency (columns 9-17, examples 4-9).

33. With respect to claim 49, although Lanza et al does not teach the use of multiple heads producing different frequencies, Kretz teaches that sound at different frequencies may be used for an examination at different depths. Particularly, regions near the surface may be examined with sound at higher frequencies than regions at larger depths. Higher sound frequencies will inherently involve a higher resolution and will also involve a lower depth of penetration into the object, which may consist of organic tissue. That lower depth of penetration may be desirable in such case as it will help to avoid ghost echoes (column 3, lines 21-47). Therefore it would be obvious to use a transducer comprising of multiple heads producing different frequencies in the method of Lanza et al, in order to allow for examination at different depths, and to avoid ghost echos.

34. With respect to claim 57, although Lanza et al teaches the use of a solid phase and a transducer (column 7, lines 35-64), he does not teach that the step of rotating the transducer around the solid phase. Kretz, however, teaches that if the wheel is rotated at constant speed and each group consists of the same number of sound transducer heads, the sound transducer heads of the group designed in accordance with the invention may be used to produce section images having a high lateral resolution. Therefore, it would be obvious to rotate the transducer in the method of Lanza et al, in order to produce section images having a high lateral resolution.

Response to Arguments

35. Applicant's arguments filed March 25, 2004 regarding the rejection of claims 50, 52, 64, 65 under 35 U.S.C. 112, first paragraph have been fully considered but are not persuasive. Applicant argues that there is no requirement under 35 U.S.C. 112, first paragraph to show why a limitation is necessary to use an invention, but rather only how to make and use an invention.

Examiner acknowledges this fact. However, it is still unclear what the purpose of the multiple heads and multiple intensities is or rather, it is unclear how multiple head or multiple intensities would be used in order to perform immunohistochemistry, in situ hybridization, fluorescent in situ hybridization, a Southern hybridization, a Northern hybridization or an ELISA. While applicant teach the use of multiple heads and intensities in ultrasound fixation or processing methods, it is unclear how these would apply to methods of performing immunohistochemistry, in situ hybridization, fluorescent in situ hybridization, a Southern hybridization, a Northern hybridization or an ELISA. Furthermore, while it is known in the prior art, to perform immunohistochemistry, in situ hybridization, fluorescent in situ hybridization, a Southern hybridization, a Northern hybridization or an ELISA, it is unclear how transducers with multiple heads or multiple intensities would be used in the methods. Therefore a person of ordinary skill in the art would not know how to perform immunohistochemistry, in situ hybridization, fluorescent in situ hybridization, a Southern hybridization, a Northern hybridization or an ELISA using a transducer with multiple heads or transducers that produce different intensities.

36. Applicant's arguments filed March 25, 2004 regarding the rejection of claims 38-40, 43, 45-48, 56, 58-64 under 35 U.S.C. 102(b) and the rejection of claims 41, 42, 44, 46-49, 51, 53-55, 57, and 69 under 35 U.S.C. 103(a) have been fully considered but they are not persuasive. Applicant argues that Lanza et al [US 5,958,371] describes ultrasound-based ELISA-type laboratory diagnostic assays in liquid and solid phase systems, not performing immunohistochemistry, in situ hybridization, fluorescent in situ hybridization, a Southern hybridization, a Northern hybridization or an ELISA. It should be noted that in applicant's method of performing immunohistochemistry, in situ hybridization, fluorescent in situ

hybridization, a Southern hybridization, a Northern hybridization, applicant only recites a single step, using ultrasound at a frequency of at least 100 kHz. Applicant does not recite any additional steps for performing the method, nor does the applicant recite any additional details on how the ultrasound will be used or the role played by ultrasound in immunohistochemistry, in situ hybridization, fluorescent in situ hybridization, a Southern hybridization, a Northern hybridization or an ELISA. Lanza et al disclose the application of ultrasonic transducers suitable for biological and diagnostic applications such as ultrasound-based ELISA-type laboratory diagnostic assays within a frequency range of at least 5 to 50 MHz (column 7, lines 35-41, 53-58). Since applicant does not recite any additional steps on how to perform the method, the method disclosed by Lanza et al would still read upon the method recited in claim 38.

37. With respect to claims 39-49, 51, 53-58, 68, 69, applicant argues that because the claims depend from claim 38 and add further distinguishing elements, the claims should be found allowable. This argument is not found persuasive for reasons discussed above regarding the rejection of claim 38.

Conclusion

38. No claims are allowed.

39. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

40. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

41. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571) 272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

42. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Nelson Yang
Patent Examiner
Art Unit 1641

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
04/19/04